CLAIMS

What is claimed is:

1. A method of treating a hyperproliferative disorder comprising administering:

a ceramide-generating anticancer agent or treatment; and

a ceramide degradation inhibitor or a pharmaceutically acceptable salt or ester thereof;

wherein the hyperproliferative disorder is a tumor; and

wherein the ceramide-generating anticancer agent or treatment is administered in an amount effective to produce necrosis, apoptosis or both in the tumor, and the ceramide degradation inhibitor is administered in an amount effective to increase the necrosis, apoptosis or both in the tumor over that expected to be produced by the sum of that produced by the ceramide-generating anticancer agent or treatment and the ceramide degradation inhibitor when administered separately.

2. The method of claim 1 wherein the ceramide degradation inhibitor comprises a compound effective in inhibiting glucosylceramide synthase and 1-O-acylceramide synthase.

3. The method of claim 2 wherein the ceramide degradation inhibitor comprises D-threo-PPMP.

4. The method of claim 3 wherein the ceramide-generating anticancer agent or treatment comprises a ceramide generating retinoid comprising a retinoic acid derivative or a pharmaceutically acceptable salt or ester thereof.

5. The method of claim 4 wherein the ceramide generating retinoid comprises fenretinide or a pharmaceutically acceptable salt or ester thereof.

6. The method of claim 5 wherein the ceramide generating retinoid and the ceramide degradation inhibitor are administered intravenously, orally, or topically.

7. A method of treating a hyperproliferative disorder comprising administering:

a ceramide-generating anticancer agent or treatment; and

a ceramide degradation inhibitor or a pharmaceutically acceptable salt thereof effective in inhibiting glucosylceramide synthase and 1-O-acylceramide synthase;

wherein the hyperproliferative disorder is a tumor; and

wherein the ceramide generating retinoid is administered in an amount effective to produce necrosis, apoptosis or both in the tumor, and the ceramide degradation inhibitor is administered in an amount effective to increase the necrosis, apoptosis or both in the tumor over that expected to be produced by the sum of that produced by the ceramide-generating anticancer agent or treatment and the ceramide degradation inhibitor when administered separately.

8. The method of claim 7 wherein the ceramide degradation inhibitor comprises D-threo-PPMP.

9. The method of claim 8 wherein the ceramide-generating anticancer agent or treatment comprises a ceramide generating retinoid comprising a retinoic acid derivative or a pharmaceutically acceptable salt or ester thereof.

10. The method of claim 9 wherein the ceramide generating retinoid comprises fenretinide or a pharmaceutically acceptable salt or ester thereof.

11. The method of claim 10 wherein the ceramide generating retinoid and the ceramide degradation inhibitor are administered intravenously, orally, or topically.

12. A method of treating a hyperproliferative disorder comprising administering:

a ceramide generating retinoid comprising fenretinide or a pharmaceutically acceptable salt or ester thereof; and

a ceramide degradation inhibitor comprising D-threo-PPMP or a pharmaceutically acceptable salt or ester thereof;

wherein the hyperproliferative disorder is a tumor; and

wherein the ceramide generating retinoid is administered in an amount effective to produce necrosis, apoptosis or both in the tumor, and the ceramide degradation inhibitor is administered in an amount effective to increase the necrosis, apoptosis or both in the tumor over that expected to be produced by the sum of that produced by the ceramide generating retinoid and the ceramide degradation inhibitor when administered separately.

13. The method of claim 12 wherein the ceramide degradation inhibitor consisting essentially of D-threo-PPMP or a pharmaceutically acceptable salt or ester thereof.

14. The method of claim 13 wherein the ceramide generating retinoid and the ceramide degradation inhibitor are administered intravenously, orally or topically.

15. A formulation for treating a hyperproliferative disorder comprising:

a ceramide-generating anticancer agent or treatment; and

a ceramide degradation inhibitor or a pharmaceutically acceptable salt or ester thereof;

wherein the hyperproliferative disorder is a tumor; and

wherein the ceramide generating anticancer agent or treatment is administered in an amount effective to produce necrosis, apoptosis or both in the tumor, and the ceramide degradation inhibitor is administered in an amount effective to increase the necrosis, apoptosis or both in the tumor over that expected to be produced by the sum of that produced by the ceramide-generating anticancer agent or treatment and the ceramide degradation inhibitor when administered separately.

16. The formulation of claim 15 wherein the ceramide degradation inhibitor comprises a compound effective in inhibiting glucosylceramide synthase and 1-O-acylceramide synthase.

17. The formulation of claim 16 wherein the ceramide degradation inhibitor comprises D-threo-PPMP or a pharmaceutically acceptable salt or ester thereof.

18. The formulation of claim 17 wherein the ceramide-generating anticancer agent or treatment comprises a ceramide generating retinoid comprising a retinoic acid derivative or a pharmaceutically acceptable salt or ester thereof.

19. The formulation of claim 18 wherein the ceramide generating retinoid comprises fenretinide or a pharmaceutically acceptable salt or ester thereof.

20. The formulation of claim 19 wherein the ceramide generating retinoid and the ceramide degradation inhibitor are administered intravenously, orally, or topically.

21. A formulation for treating a hyperproliferative disorder comprising:

a ceramide generating retinoid comprising fenretinide or a pharmaceutically acceptable salt or ester thereof; and

a ceramide degradation inhibitor comprising D-threo-PPMP or a pharmaceutically acceptable salt or ester thereof;

wherein the hyperproliferative disorder is a tumor; and

wherein the ceramide generating retinoid is administered in an amount effective to produce necrosis, apoptosis or both in the tumor and the ceramide degradation inhibitor is administered in an amount effective to increase the necrosis, apoptosis or both in the tumor over that expected to be produced by the sum of that produced by the ceramide generating retinoid and the ceramide degradation inhibitor when administered separately.

22. The formulation of claim 21 wherein the ceramide degradation inhibitor consisting essentially of D-threo-PPMP or a pharmaceutically acceptable salt or ester thereof.

23. The formulation of claim 21 wherein said formulation is administered intravenously, orally, or topically.

24. A method of treating a hyperproliferative disorder comprising administering:

a ceramide-generating anticancer agent or treatment; and

a ceramide degradation inhibitor wherein said ceramide degradation inhibitor comprises D-threo-PPMP or a pharmaceutically acceptable salt or ester thereof;

wherein the hyperproliferative disorder is a tumor; and

wherein the ceramide-generating anticancer agent or treatment is administered in an amount effective to produce necrosis, apoptosis or both in the tumor, and D-threo-PPMP is administered in an amount effective to increase the necrosis, apoptosis or both in the tumor over that expected to be produced by the sum of that produced by the ceramide-generating anticancer agent or treatment and D-threo-PPMP when administered separately.

25. The method of claim 24 wherein the ceramide degradation inhibitor consisting essentially of D-threo-PPMP or a pharmaceutically acceptable salt or ester thereof.

26. A formulation for treating a hyperproliferative disorder comprising:

a ceramide-generating anticancer agent or treatment; and

a ceramide degradation inhibitor wherein said ceramide degradation inhibitor comprises D-threo-PPMP or a pharmaceutically acceptable salt or ester thereof;

wherein the hyperproliferative disorder is a tumor; and

wherein the ceramide-generating anticancer agent or treatment is administered in an amount effective to produce necrosis, apoptosis or both in the tumor, and D-threo-PPMP is administered in an amount effective to increase the necrosis, apoptosis or both in the tumor over that expected to be produced by the sum of that produced by the ceramide-generating anticancer agent or treatment and D-threo-PPMP when administered separately.

27. The formulation of claim 26 wherein the ceramide degradation inhibitor consisting essentially of D-threo-PPMP or a pharmaceutically acceptable salt or ester thereof.

28. A method of treating a hyperproliferative disorder comprising administering:

a ceramide-generating anticancer agent or treatment; and

a ceramide degradation inhibitor wherein said ceramide degradation inhibitor comprises a single isomer that is effective in inhibiting both glucosylceramide synthase and 1-O-acylceramide synthase;

wherein the hyperproliferative disorder is a tumor; and

wherein the ceramide-generating anticancer agent or treatment is administered in an amount effective to produce necrosis, apoptosis or both in the tumor, and the ceramide degradation inhibitor is administered in an amount effective to increase the necrosis, apoptosis or both in the tumor over that expected to be produced by the sum of that produced by the ceramide-generating anticancer agent or treatment and the ceramide degradation inhibitor when administered separately.

29. The method of claim 28 wherein the isomer comprises D-threo-PPMP or a pharmaceutically acceptable salt or ester thereof.

30. The method of claim 29 wherein the ceramide-generating anticancer agent or treatment comprises a ceramide generating retinoid comprising a retinoic acid derivative or a pharmaceutically acceptable salt or ester thereof.

31. The method of claim 30 wherein the ceramide generating retinoid comprises fenretinide or a pharmaceutically acceptable salt or ester thereof.

32. The method of claim 31 wherein the ceramide generating retinoid and the ceramide degradation inhibitor are administered intravenously, orally, or topically.